R^8 represents hydrogen, halo, (C_1-C_6) alkyl, hydroxy (C_1-C_6) alkyl, (C_1-C_4) alkyl - (C_1-C_6) alkoxy, COR^{12} wherein R^{12} represents methoxy, ethoxy, hydroxymethyl, or methoxymethyl; (C_3-C_7) cycloalkyl, aryl or substituted aryl.

37. A novel compound of Formula I:

Formula I

wherein,

A, B, and C each independently represent an aryl, heterocycle, or benzofusedheterocyclic ring;

X and Y together represent $-CH_2-CH_2-$, -CH=CH-, $-CH_2-O-$, $-O-CH_2-$, $-CH_2-S-$, $-S-CH_2-$, $-CH_2-SO-$, $-SO-CH_2-$, $-CH_2-SO_2-$, $-SO_2-CH_2-$, $-CH_2-NR^{10}-$, $-NR^{10}-CH_2-$, $-NR^{10}-CO-$, $-CO-NR^{10}-$, or a group of the formula

15 formula

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$$W$$
 or W' Z'

wherein W and Z each independently represent hydrogen, fluoro, or chloro; W' and Z' each independently represent hydrogen, fluoro, chloro, or methyl; and Q represents NH, O, S, or CH₂;

"_---" represents a single or double bond;

 R^1 represents hydrogen, halo, hydroxy, cyano, nitro, amino, oxo, $(C_1\text{-}C_6)$ alkyl, $(C_1\text{-}C_6)$ alkoxy, hydroxy $(C_1\text{-}C_6)$ alkyl, hydroxy $(C_1\text{-}C_6)$ alkoxy, $(C_2\text{-}C_6)$ alkenyl, $(C_2\text{-}C_6)$ alkynyl, $C_2\text{-}C_6$ alkynyl, halo $(C_1\text{-}C_6)$ alkoxy, $C_2\text{-}C_6$ alkoxy, $C_2\text{-}C_6$ alkynyl, $C_2\text{-}C_6$ alkyl, halo $(C_1\text{-}C_6)$ alkoxy, $C_2\text{-}C_6$ alkoxy, $C_2\text{-}C_6$ alkynyl, $C_2\text{-}C_6$ alkynyl, $C_2\text{-}C_6$ alkoxy, $C_2\text{-}C_6$ alko

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substituted aryl, (C_1-C_4) alkyl-aryl, (C_1-C_4) alkyl-substituted aryl, heterocycle, substituted heterocycle, (C_1-C_4) alkyl-heterocycle, or (C_1-C_4) alkyl-substituted heterocycle;

provided that where "C" represents an aryl group, R^1 is other than oxo, (C₂-C₆)alkenyl, or (C₂-C₆)alkynyl;

further provided that where "C" represents a benzo-fused heterocycle then R¹ may also represent hydrogen;

 R^2 through R^8 each independently represent hydrogen, halo, hydroxy, cyano, nitro, amino, $(C_1\text{-}C_6)$ alkyl, $(C_1\text{-}C_6)$ alkoxy, hydroxy $(C_1\text{-}C_6)$ alkyl, hydroxy $(C_1\text{-}C_6)$ alkoxy, $(C_2\text{-}C_6)$ alkenyl, $(C_2\text{-}C_6)$ alkynyl, $C_2\text{-}C_6)$ alkynyl, $C_2\text{-}C_6)$ alkynyl, $C_2\text{-}C_6)$ alkynyl, $C_2\text{-}C_6)$ alkyl, halo $(C_1\text{-}C_6)$ alkoxy, $C_2\text{-}C_6)$ alkynyl, $C_2\text{-}C_6)$ alkynyl, $C_2\text{-}C_6)$ alkyl, halo $(C_1\text{-}C_6)$ alkoxy, $C_2\text{-}C_6)$ alkyl, $C_2\text{-}C_6)$ alkoxy, $C_2\text{-}C_6)$ alkyl, $C_2\text{-}C_6$ alkyl, $C_2\text{-}C_6$ alkyl, $C_2\text{-}C_6$ alkyl, $C_2\text{-}C_6$ alkyl, aryl, substituted aryl, $C_2\text{-}C_4$ alkyl- $C_2\text{-}C_6$ alkoxy, $C_2\text{-}C_4$ alkyl-aryl, $C_2\text{-}C_4$ alkyl-substituted aryl, heterocycle, substituted heterocycle, $C_2\text{-}C_4$ alkyl-heterocycle, or $C_2\text{-}C_4$ alkyl-substituted heterocycle;

provided that where "A", "B", or "C" represents an aryl group, each of \mathbb{R}^2 through \mathbb{R}^7 is other than (C₂-C₆)alkenyl or (C₂-C₆)alkynyl;

further provided that where C represents a phenyl ring and R¹ represents halo then at least one of R² and R³ is other than hydrogen, (C₁-C₆)alkyl, aryl, substituted aryl, (C₁-C₄)alkyl-aryl, (C₁-C₄)alkyl-substituted aryl, CHF₂, or CF₃;

further provided that where C represents a six-membered ring and R¹ represents cyano, amino, NR⁹R¹⁰, or NHCOCH₃ and R² and R³ are each hydrogen, then R¹ is not bound at the 4-position of said six-membered ring;

further provided that where C represents a six-membered ring and R¹ represents nitro, and R² and R³ are each hydrogen, then R¹ is not bound at the 2, 4, or 6-position of said six-membered ring;

 R^9 represents independently at each occurrence cyano, $(C_1\text{-}C_6)$ alkyl, $(C_1\text{-}C_6)$ alkoxy, $(C_1\text{-}C_4)$ alkyl- $(C_1\text{-}C_6)$ alkoxy, halo $(C_1\text{-}C_6)$ alkyl, hydroxy $(C_1\text{-}C_6)$ alkyl, $(C_3\text{-}C_7)$ cycloalkyl, NH- $(C_1\text{-}C_6)$ alkylamine, N,N- $(C_1\text{-}C_6)$ dialkylamine, aryl, substituted aryl, $(C_1\text{-}C_4)$ alkyl-aryl, $(C_1\text{-}C_4)$ alkyl-substituted aryl, heterocycle, substituted heterocycle, $(C_1\text{-}C_4)$ alkyl-heterocycle, or $(C_1\text{-}C_4)$ alkyl-substituted heterocycle;

R¹⁰ represents independently at each occurrence hydrogen or (C₁-C₆)alkyl

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-432-



or \mathbb{R}^9 and \mathbb{R}^{10} together with the nitrogen atom to which they are attached, form a substituted or unsubstituted heterocycle group;

R¹¹ represents independently at each occurrence amino, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, halo(C₁-C₆)alkyl, (C₃-C₇)cycloalkyl, aryl, substituted aryl, (C₁-C₄)alkyl-aryl, (C₁-C₄)alkyl-substituted aryl, heterocycle, substituted heterocycle, (C₁-C₄)alkyl-heterocycle, or (C₁-C₄)alkyl-substituted heterocycle;

 R^{12} represents independently at each occurrence hydrogen, amino, (C_1-C_6) alkyl, hydroxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkyl-(C_1-C_6)alkoxy, (C_3-C_7)cycloalkyl, NH-(C_1-C_6)alkylamine, N,N-(C_1-C_6)dialkylamine, aryl, substituted aryl, (C_1-C_4)alkyl-aryl, (C_1-C_4)alkyl-substituted aryl, heterocycle, substituted heterocycle, (C_1-C_4)alkyl-heterocycle, or (C_1-C_4)alkyl-substituted heterocycle;

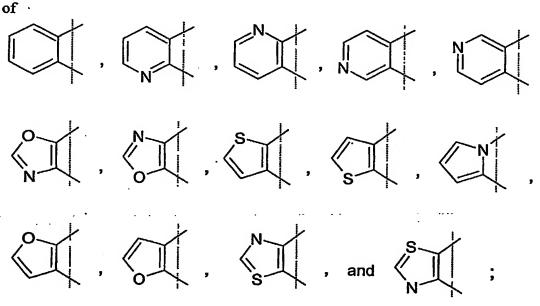
R¹³ represents independently at each occurrence OH, (C₁-C₆)alkyl, (C₃-C₇)cycloalkyl, aryl, heterocycle, or a substituted aryl or heterocycle;

 R^{14} represents independently at each occurrence (C₃-C₇)cycloalkyl, aryl, substituted aryl, acyl, (C₁-C₄)alkyl-aryl, (C₁-C₄)alkyl-substituted aryl, heterocycle, substituted heterocycle, (C₁-C₄)alkyl-heterocycle, (C₁-C₄)alkyl-substituted heterocycle, or (C₁-C₄)alkyl-(C₃-C₇)cycloalkyl;

or a pharmaceutically acceptable salt thereof.

20 38. The compound according to Claim 37 wherein the compound of Formula I is one wherein,

"A" represents an aryl or heterocycle ring selected from the group consisting



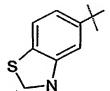
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"B" represents an aryl or heterocyclic ring selected from the group consisting

"C" represents an aryl, heterocyclic, or benzofused heterocycle ring selected from the group consisting of

and



or a pharmaceutically acceptable salt thereof.

The compound according to claim 38 wherein "A" represents 39.

"B" represents

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or
$$N = N$$

or a pharmaceutically acceptable salt thereof.

- 40. A compound according to any one of claims 37-39 wherein X-Y represents $-CH_2$ —, $-CH_2$ —, or $-CH_2$ —, or $-CH_2$ —, or $-CH_2$ —, or $-CH_2$ —.
- 41. The compound according to Claim 40 wherein X-Y represents $-CH_2$ — CH_2 -, $-CH_2$ —O-, -O- CH_2 -, $-CH_2$ -, or $-CH_2$ -, wherein R10 represents hydrogen or methyl.
- 42. The compound according to Claim 41 wherein X-Y represents -CH₂—. CH₂—, -CH₂—O-, or -O—CH₂—.
- 43. A compound according to any one of Claims 37-42 wherein "----" represents a double bond.
- 44. A compound according to any one of Claims 37-43 wherein R^1 represents hydrogen, halo, hydroxy, cyano, nitro, amino, oxo $(C_1\text{-}C_6)$ alkyl, $(C_1\text{-}C_6)$ alkoxy, hydroxy $(C_1\text{-}C_6)$ alkyl, CH_2NH_2 , halo $(C_1\text{-}C_6)$ alkyl, halo $(C_1\text{-}C_6)$ alkoxy, SO_2NH_2 , $SO_2NR^9R^{10}$, SO_2R^{11} , NH SO_2R^{11} , NR^9R^{10} , $NHCOR^{12}$, COR^{12} , $CHNR^{13}$, OR^{14} , SR^{14} , heterocycle, $(C_1\text{-}C_4)$ alkyl-heterocycle, or substituted heterocycle, provided that where "C" represents an aryl group then R^1 is other than oxo.
- 45. The compound according to Claims 44 wherein R^1 represents halo, amino, oxo, $(C_1\text{-}C_6)$ alkyl, $(C_1\text{-}C_6)$ alkoxy, hydroxymethyl, difluromethyl, trifluoromethyl, difluromethoxy, trifluoromethoxy, $SO_2NR^9R^{10}$, NH SO_2R^{11} , NHCOR¹², COR¹², OR¹⁴, or $(C_1\text{-}C_4)$ alkyl-heterocycle, provided that where "C" represents an aryl group then R^1 is other than oxo.
- 46. The compound according to Claim 45 wherein when R^1 represents $SO_2NR^9R^{10}$, R^9 represents (C_1-C_6) alkyl, (C_1-C_4) alkyl- (C_1-C_6) alkoxy, halo (C_1-C_6) alkyl, (C_3-C_7) cycloalkyl, aryl, (C_1-C_4) alkyl-aryl, heterocycle and R^{10} represents hydrogen or methyl, or R^9 and R^{10} together with the nitrogen to which they are attached form a substituted or unsubstituted heterocycle:

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47. The compound according to Claim 45 wherein when R^1 represents NH SO_2R^{11} , R^{11} represents amino, (C_1-C_6) alkyl, halo (C_1-C_6) alkyl, (C_1-C_6) alkoxy, (C_3-C_7) cycloalkyl, aryl, substituted aryl, heterocycle, or substituted heterocycle.

-436-

- 48. The compound according to Claim 47 wherein R¹¹ represents methyl, ethyl, propyl, isopropyl, butyl, or 2-methyl propyl.
- 49. The compound according to Claim 45 wherein when R^1 represents NHCOR¹², R^{12} represents H, amino, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, hydroxy(C₁-C₆)alkyl, (C₁-C)alkyl-(C₁-C₆)alkoxy, halo(C₁-C₆)alkyl, NH-methylamine, NH-dimethylamine, NH-ethylamine, or heterocycle.
- 50. The compound according to Claim 45 wherein when R¹ represents COR¹², R¹² represents H, amino, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, or hydroxy(C₁-C₆)alkyl.
- 51. The compound according to Claim 45 wherein when R^1 represents OR^{14} , R^{14} represents (C_1-C) alkyl-heterocycle.
- 52. The compound according to Claim 45 wherein (C₁-C)alkyl-heterocycle represents a group of the formula

$$\sim$$
 or \sim \sim \sim \sim

- 53. A compound according to any one of Claims 37-52 wherein R² represents hydrogen, halo, hydroxy, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, halo(C₁-C₆)alkyl, (C₃-. C₇)cycloalkyl, or (C₁-C₄)alkyl-heterocycle.
- 54. The compound according to Claim 53 wherein R² represents hydrogen or (C₁-C₄)alkyl-heterocycle.
 - 55. The compound according to Claim 54 wherein R² represents hydrogen.
- 56. A compound according to any one of Claims 37-55 wherein \mathbb{R}^3 represents 25 hydrogen, halo, or (C_1-C_6) alkyl.
 - 57. The compound according to Claim 56 wherein R³ represents hydrogen.
 - 58. A compound according to any one of Claims 37-57 wherein R⁴-R⁷ each independently represent hydrogen, halo, hydroxy, cyano, amino, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, halo(C₁-C₆)alkyl, halo(C₁-C₆)alkoxy, SO₂NH₂, SO₂CH₃, NH SO₂R¹¹, NR⁹R¹⁰, NHCOR¹², COR¹², OR¹⁴, SR¹⁴, or aryl.
 - 59. The compound according to Claim 58 wherein R⁴-R⁷ each independently represent hydrogen, halo, hydroxy, cyano, amino, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, CHF₂, CF₃, OCHF₂, OCF₃, NH SO₂R¹¹, NR⁹R¹⁰, NHCOR¹², COR¹², OR¹⁴, or aryl.

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60. The compound according to Claim 59 wherein R⁴-R⁷ each independently represent hydrogen, halo, hydroxy, cyano, amino, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, CHF₂, CF₃, OCHF₂, OCF₃, NH SO₂CH₃, dimethylamine, NHCOCH₃, COR¹² wherein R¹² represents hydrogen, amino, or methoxy; OR¹⁴ wherein R¹⁴ represents (C₁-C₄)alkylaryl, (C₁-C₄)alkyl-substituted aryl, (C₁-C₄)alkyl-heterocycle, or (C₁-C₄)alkyl-(C₃-C₇)cycloalkyl; or aryl.

-437-

- 61. The compound according to Claim 60 wherein R^4 - R^7 each independently represent hydrogen, hydroxy, halo, $(C_1$ - C_6)alkyl, $(C_1$ - C_6)alkoxy, or OR^{14} wherein R^{14} represents $(C_1$ - C_4)alkyl-aryl, $(C_1$ - C_4)alkyl-substituted aryl, $(C_1$ - C_4)alkyl-heterocycle, or $(C_1$ - C_4)alkyl- $(C_3$ - C_7)cycloalkyl.
- 62. The compound according to Claim 61 wherein R^4 and R^6 each independently represent hydrogen, halo, (C_1-C_6) alkyl, (C_1-C_6) alkoxy, or OR^{14} wherein R^{14} represents (C_1-C_4) alkyl-aryl, (C_1-C_4) alkyl-substituted aryl, (C_1-C_4) alkyl-heterocycle, or (C_1-C_4) alkyl- (C_3-C_7) cycloalkyl.
- 63. The compound according to Claim 61 wherein R⁵ and R⁷ each independently represent hydrogen, hydroxy, halo, (C₁-C₆)alkyl, or (C₁-C₆)alkoxy.
- 64. A compound according to any one of Claims 37-63 wherein R^8 represents hydrogen, halo, (C_1-C_6) alkyl, hydroxy (C_1-C_6) alkyl, (C_1-C_4) alkyl - (C_1-C_6) alkoxy, COR^{12} , (C_3-C_7) cycloalkyl, aryl, or substituted aryl.
- 65. The compound according to Claim 64 wherein R⁸ represents hydrogen, halo, (C₁-C₆)alkyl, hydroxymethyl, (C₁-C₄)alkyl -(C₁-C₆)alkoxy, COR¹² wherein R¹² represents (C₁-C₆)alkoxy; (C₃-C₇)cycloalkyl, phenyl, or substituted aryl.
- 66. The compound according to Claim 65 wherein R⁸ represents hydrogen, halo, (C₁-C₆)alkyl, (C₁-C₄)alkyl -(C₁-C₆)alkoxy, or (C₃-C₇)cycloalkyl.
- 25 67. The compound according to Claim 66 wherein R⁸ represents halo (C₁-C₆)alkyl, (C₁-C₄)alkyl -(C₁-C₆)alkoxy.
 - 68. The compound according to Claim 66 wherein R⁸ represents hydrogen.
 - 69. The compound according to Claim 37 wherein
 - "A" and "B" each independently represent phenyl or heterocycle;
- X and Y together represent $-CH_2$ CH_2 —, -CH=CH—, $-CH_2$ —O—, -O— CH_2 —, $-CH_2$ —S—, -S— CH_2 —, $-CH_2$ —SO—, -SO— CH_2 —, $-CH_2$ —SO—, -SO— CH_2 —, $-CH_2$ — $-CH_2$ — $-CH_2$ —, $-CH_2$ — $-CH_2$ —, $-CH_2$ —, or a group of the formula



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wherein W and Z each independently represent hydrogen, fluoro, or chloro;

"----" represents a single or double bond;

R¹ represents halo, hydroxy, cyano, nitro, amino, oxo, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, hydroxy(C₁-C₆)alkyl, CH₂NH₂, halo(C₁-C₆)alkyl, halo(C₁-C₆)alkoxy, SO₂NH₂, SO₂NR⁹R¹⁰ wherein R⁹ represents (C₁-C₆)alkyl, halo(C₁-C₆)alkyl, (C₁-C₄)alkyl-(C₁-C₆)alkoxy, aryl, (C₁-C₄)alkyl-aryl, (C₃-C₇)cycloalkyl and R¹⁰ represents hydrogen or (C₁-C₆)alkyl or R⁹ and R¹⁰ together represent a substituted or unsubstituted heterocycle; SO₂R¹¹ wherein R11 represents (C₁-C₆)alkyl; NH SO₂R¹¹ wherein R¹¹ represents (C₁-C₆)alkyl, halo(C₁-C₆)alkyl, (C₃-C₇)cycloalkyl, aryl, substituted aryl, heterocycle, or substituted heterocycle; NR⁹R¹⁰ wherein R⁹ represents (C₁-C₆)alkyl or cyano and R¹⁰ represents hydrogen or methyl; NHCOR¹² wherein R¹² represents H, amino, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, hydroxy(C₁-C₆)alkyl, (C₁-C₆)alkyl-(C₁-C₆)alkoxy, halo(C₁-C₆)alkyl, NH-methylamine,NH-ethylamine, or heterocycle; COR¹² wherein R¹² represents H, amino, (C₁-C₆)alkyl, (C₁-C₆)alkyl, (C₁-C₆)alkyl; OR¹⁴ wherein R¹⁴ represents (C₁-C₆)alkyl-heterocycle or acetyl; SR¹⁴ wherein R¹⁴ represents (C₁-C₆)alkyl; heterocycle, (C₁-C₄)alkyl-heterocycle, or substituted heterocycle,

provided that where "C" represents an aryl group then R¹ is other than oxo; further provided that where "C" represents a benzo-fused heterocycle then R¹ may also represent hydrogen;

R² represents hydrogen, halo, hydroxy, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, halo(C₁-C₆)alkyl, (C₃-C₇)cycloalkyl, or (C₁-C₄)alkyl-heterocycle;

R³ represents wherein hydrogen, halo, or (C₁-C₆)alkyl;

provided that where C represents a phenyl ring and R^1 represents halo then at least one of R^2 and R^3 is other than hydrogen, (C_1-C_6) alkyl, aryl, substituted aryl, (C_1-C_4) alkyl-aryl, (C_1-C_4) alkyl-substituted aryl, CHF₂, or CF₃;

further provided that where C represents a six-membered ring and R^1 represents cyano, amino, NR^9R^{10} , or $NHCOCH_3$ and R^2 and R^3 are each hydrogen, then R^1 is not bound at the 4-position of said six-membered ring;

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further provided that where C represents a six-membered ring and R^1 represents nitro, and R^2 and R^3 are each hydrogen, then R^1 is not bound at the 2, 4, or 6-position of said six-membered ring;

R⁴ and R⁶ each independently represent hydrogen, halo, hydroxy, cyano, amino, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, halo(C₁-C₆)alkyl, hydroxymethyl, SO₂CH₃, NH SO₂R¹¹ wherein R11 represents (C₁-C₆)alkyl; NR⁹R¹⁰ wherein R⁹ and R¹⁰ each represent (C₁-C₆)alkyl, NHCOR¹² wherein R¹² represents (C₁-C₆)alkyl; COR¹² wherein R¹² represents hydrogen, amino, or (C₁-C₆)alkoxy; OR¹⁴ wherein R¹⁴ represents (C₁-C₄)alkyl-(C₃-C₇)cycloalkyl, (C₁-C₄)alkyl-aryl, (C₁-C₄)alkyl-substituted aryl, or (C₁-C₄)alkyl-heterocycle; SR¹⁴ wherein R¹⁴ represents (C₁-C₆)alkyl; or aryl;

 R^5 and R^7 each independently represent hydrogen, hydroxy, halo, (C_1 - C_6)alkyl, or (C_1 - C_6)alkoxy; and

 R^8 represents hydrogen, halo, (C₁-C₆)alkyl, hydroxy(C₁-C₆)alkyl, (C₁-C₄)alkyl - (C₁-C₆)alkoxy, COR¹² wherein R^{12} represents methoxy, ethoxy, hydroxymethyl, or methoxymethyl; (C₃-C₇)cycloalkyl, aryl or substituted aryl.

70. A compound of the formula

or a pharmaceutically acceptable salt thereof.

or a pharmaceutically acceptable salt thereof.

72. A compound of the formula

- 5 or a pharmaceutically acceptable salt thereof.
 - 73. A compound of the formula

- or a pharmaceutically acceptable salt thereof.
 - 74. A compound of the formula

or a pharmaceutically acceptable salt thereof.

75. A compound of the formula

or a pharmaceutically acceptable salt thereof.

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76. A compound of the formula

or a pharmaceutically acceptable salt thereof.

77. A compound of the formula

or a pharmaceutically acceptable salt thereof.

78. A compound of the formula

or a pharmaceutically acceptable salt thereof.

or a pharmaceutically acceptable salt thereof.

80. A compound of the formula

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or a pharmaceutically acceptable salt thereof.

- or a pharmaceutically acceptable salt thereof.
 - 82. A compound of the formula...

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or a pharmaceutically acceptable salt thereof.

83. A compound of the formula

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or a pharmaceutically acceptable salt thereof.

- or a pharmaceutically acceptable salt thereof.
 - 85. A compound of the formula

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or a pharmaceutically acceptable, salt thereof.

86. A compound of the formula

or a pharmaceutically acceptable salt thereof.

- or a pharmaceutically acceptable salt thereof.
 - 88. A compound of the formula

APP COMMENT

or a pharmaceutically acceptable salt thereof.

89. A compound of the formula

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or a pharmaceutically acceptable salt thereof.

- or a pharmaceutically acceptable salt thereof.
 - 91. A compound of the formula

or a pharmaceutically acceptable salt thereof.

92. A compound of the formula

or a pharmaceutically acceptable salt thereof.

- or a pharmaceutically acceptable salt thereof.
 - 94. A compound of the formula

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or a pharmaceutically acceptable salt thereof.

95. A compound of the formula

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or a pharmaceutically acceptable salt thereof.

- or a pharmaceutically acceptable salt thereof.
 - 97. A compound of the formula

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or a pharmaceutically acceptable salt thereof.

98. A compound of the formula

or a pharmaceutically acceptable salt thereof.

- or a pharmaceutically acceptable salt thereof.
 - 100. A compound of the formula

or a pharmaceutically acceptable salt thereof.

101. A compound of the formula

or a pharmaceutically acceptable salt thereof.

- or a pharmaceutically acceptable salt thereof.
 - 103. A compound of the formula

-450-

or a pharmaceutically acceptable salt thereof.

104. A compound of the formula

or a pharmaceutically acceptable salt thereof.

105. A compound of the formula

or a pharmaceutically acceptable salt thereof.



-451-

or a pharmaceutically acceptable salt thereof.

107. A compound of the formula

or a pharmaceutically acceptable salt thereof.

- or a pharmaceutically acceptable salt thereof.
 - 109. A compound of the formula





or a pharmaceutically acceptable salt thereof.

110. A compound of the formula

or a pharmaceutically acceptable salt thereof.

- or a pharmaceutically acceptable salt thereof.
 - 112. A compound of the formula







-453-

or a pharmaceutically acceptable salt thereof.

- 113. A method of treating a physiological disorder susceptible to steroid hormone nuclear receptor modulation comprising administering to a patient in need thereof effective amount of a novel compound of Formula I according to claim 37.
- 114. The method according to claim 113 wherein said disorder is susceptible to mineralocorticoid or glucocorticoid receptor modulation.
- 115. The method according to Claim 114 wherein said disorder is selected from the group consisting of Conn's Syndrome, primary and secondary hyperaldosteronism, 10 increased sodium retention, increased magnesium and potassium excretion (diuresis), increased water retention, hypertension (isolated systolic and combined systolic/diastolic), arrhythmias, myocardial fibrosis, myocardial infarction, Bartter's Syndrome, disorders associated with excess catecholamine levels, diastolic and systolic 15 congestive heart failure (CHF), psychoses, cognitive disorders, memory disturbances, depression, bipolar disorder, anxiety disorders, personality disorders, breast cancer, peripheral vascular disease, diabetic nephropathy, cirrhosis with edema and ascites, esophageal varicies, Addison's Disease, muscle weakness, increased melanin pigmentation of the skin, weight loss, hypotension, hypoglycemia, Cushing's Syndrome, 20 obesity, hypertension, glucose intolerance, hyperglycemia, diabetes mellitus, osteoporosis, polyuria, polydipsia, inflammation, autoimmune disorders, tissue rejection associated with organ transplant, malignancies such as leukemias and lymphomas, acute adrenal insufficiency, congenital adrenal hyperplasia, rheumatic fever, polyarteritis nodosa, granulomatous polyarteritis, inhibition of myeloid cell lines, immune proliferation/apoptosis, HPA axis suppression and regulation, hypercortisolemia, 25 modulation of the Th1/Th2 cytokine balance, chronic kidney disease, stroke and spinal cord injury, hypercalcemia, hypergylcemia, acute adrenal insufficiency, chronic primary adrenal insufficiency, secondary adrenal insufficiency, congenital adrenal hyperplasia,



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cerebral edema, thrombocytopenia, and Little's syndrome, systemic inflammation, inflammatory bowel disease, systemic lupus erythematosus, discoid lupus erythematosus, polyartitis nodosa, Wegener's granulomatosis, giant cell arthritis, rheumatoid arthritis, osteoarthritis, hay fever, allergic rhinitis, contact dermatitis, atopic dermatitis, exfoliative dermatitis, urticaria, angioneurotic edema, chronic obstructive pulmonary disease, asthma, tendonitis, bursitis, Crohn's disease, ulcerative colitis, autoimmune chronic active hepatitis, hepatitis, cirrhosis, inflammatory scalp alopecia, panniculitis, psoriasis, inflamed cysts, pyoderma gangrenosum, pemphigus vulgaris, bullous pemphigoid, dermatomyositis, eosinophilic fasciitis, relapsing polychondritis, inflammatory vasculitis, sarcoidosis, Sweet's disease, type 1 reactive leprosy, capillary hemangiomas, lichen planus, , erythema nodosum, acne, hirsutism, toxic epidermal necrolysis, erythema multiform, cutaneous T-cell lymphoma, emphysema, Alzheimer's Disease, and multiple sclerosis.

- 116. The method according to claim 115, wherein said disorder is diastolic or systolic congestive heart failure, inflammation, rheumatoid arthritis, an autoimmune disorder, asthma, or chronic obstructive pulmonary disease.
- 117. The method according to claim 116, wherein said disorder is diastolic or systolic congestive heart failure or rheumatoid arthritis.
- 118. A method of modulating a steroid hormone nuclear receptor comprising administering to a patient in need thereof an effective amount of a compound of Formula I according to Claim 37.
- 119. The method of Claim 118 wherein said steroid nuclear receptor is the mineralocorticoid receptor or the glucocorticoid receptor.
- 120. A pharmaceutical composition comprising an effective amount of a compound of Formula I according to Claim 37 in combination with a pharmaceutically acceptable carrier.
 - 121. The use of a compound of Formula I:





Formula I

wherein,

WO 2004/052847

A, B, and C each independently represent an aryl, heterocycle, or benzofusedheterocyclic ring;

 $X \ and \ Y \ together \ represent - CH_2 -- CH_2 -- , -CH = CH_-, -CH_2 -- O_-, -O_- CH_2 -- , -CH_2 -- S_-, -S_- CH_2 -- , -CH_2 -- S_-, -S_- CH_2 -- , -CH_2 -- S_-, -CH_2 -- S_-,$

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wherein W and Z each independently represent hydrogen, fluoro, or chloro; W' and Z' each independently represent hydrogen, fluoro, chloro, or methyl; and Q represents NH, O, S, or CH₂;

"----" represents a single or double bond;

 R^1 represents hydrogen, halo, hydroxy, cyano, nitro, amino, oxo, $(C_1\text{-}C_6)$ alkyl, $(C_1\text{-}C_6)$ alkoxy, hydroxy $(C_1\text{-}C_6)$ alkyl, hydroxy $(C_1\text{-}C_6)$ alkoxy, $(C_2\text{-}C_6)$ alkenyl, $(C_2\text{-}C_6)$ alkynyl, CH_2NH_2 , halo $(C_1\text{-}C_6)$ alkyl, halo $(C_1\text{-}C_6)$ alkoxy, $C(CF_3)_2OH$, SO_2NH_2 , $SO_2NR^9R^{10}$, SO_2R^{11} , $NHSO_2R^{11}$, $N(CH_3)SO_2CH_3$, NR^9R^{10} , $CH_2NH(OH)$, $CH_2NH(SO_2R^{11})$, $NHCOR^{12}$, COR^{12} , $CHNR^{13}$, OR^{14} , SR^{14} , $(C_3\text{-}C_7)$ cycloalkyl, aryl, substituted aryl, $(C_1\text{-}C_4)$ alkyl-aryl, $(C_1\text{-}C_4)$ alkyl-substituted heterocycle, substituted heterocycle;

provided that where "C" represents an aryl group, R^1 is other than oxo, (C₂-C₆)alkenyl, or (C₂-C₆)alkynyl;

 R^2 through R^8 each independently represent hydrogen, halo, hydroxy, cyano, nitro, amino, (C_1-C_6) alkyl, (C_1-C_6) alkoxy, hydroxy (C_1-C_6) alkoxy,

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 (C_2-C_6) alkenyl, (C_2-C_6) alkynyl, CH_2NH_2 , halo (C_1-C_6) alkyl, halo (C_1-C_6) alkoxy, $C(CF_3)_2OH$, SO_2NH_2 , $SO_2NR^9R^{10}$, SO_2R^{11} , $NHSO_2R^{11}$, NR^9R^{10} , $CH_2NH(OH)$, $CH_2NH(SO_2R^{11})$, $NHCOR^{12}$, COR^{12} , $CHNR^{13}$, OR^{14} , SR^{14} , (C_3-C_7) cycloalkyl, aryl, substituted aryl, (C_1-C_4) alkyl- (C_1-C_6) alkoxy, (C_1-C_4) alkyl-aryl, (C_1-C_4) alkyl-substituted aryl, heterocycle, substituted heterocycle, (C_1-C_4) alkyl-heterocycle, or (C_1-C_4) alkyl-substituted heterocycle;

provided that where "A", "B", or "C" represents an aryl group, each of \mathbb{R}^2 through \mathbb{R}^7 is other than $(\mathbb{C}_2\text{-}\mathbb{C}_6)$ alkenyl or $(\mathbb{C}_2\text{-}\mathbb{C}_6)$ alkynyl;

R⁹ represents independently at each occurrence cyano, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, (C₁-C₄)alkyl-(C₁-C₆)alkoxy, halo(C₁-C₆)alkyl, hydroxy(C₁-C₆)alkyl, (C₃-C₇)cycloalkyl, NH-(C₁-C₆)alkylamine, N,N-(C₁-C₆)dialkylamine, aryl, substituted aryl, (C₁-C₄)alkyl-aryl, (C₁-C₄)alkyl-substituted aryl, heterocycle, substituted heterocycle, (C₁-C₄)alkyl-heterocycle, or (C₁-C₄)alkyl-substituted heterocycle;

R¹⁰ represents independently at each occurrence hydrogen or (C₁-C₆)alkyl or R⁹ and R¹⁰ together with the nitrogen atom to which they are attached, form a substituted or unsubstituted heterocycle group;

 R^{11} represents independently at each occurrence amino, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, halo(C₁-C₆)alkyl, (C₃-C₇)cycloalkyl, aryl, substituted aryl, (C₁-C₄)alkyl-aryl, (C₁-C₄)alkyl-substituted aryl, heterocycle, substituted heterocycle, (C₁-C₄)alkyl-heterocycle, or (C₁-C₄)alkyl-substituted heterocycle;

 R^{12} represents independently at each occurrence hydrogen, amino, (C₁-C₆)alkyl, hydroxy(\dot{C}_1 -C₆)alkyl, halo(C_1 -C₆)alkyl, (C_1 -C₆)alkoxy, (C_1 -C₆)alkyl-(C_1 -C₆)alkyl-(C_1 -C₆)alkyl-aryl, NH-(C_1 -C₆)alkylamine, N,N-(C_1 -C₆)dialkylamine, aryl, substituted aryl, (C_1 -C₄)alkyl-aryl, (C_1 -C₄)alkyl-substituted aryl, heterocycle, substituted heterocycle, (C_1 -C₄)alkyl-heterocycle, or (C_1 -C₄)alkyl-substituted heterocycle;

R¹³ represents independently at each occurrence OH, (C₁-C₆)alkyl, (C₃-C₇)cycloalkyl, aryl, heterocycle, or a substituted aryl or heterocycle;

R¹⁴ represents independently at each occurrence (C₃-C₇)cycloalkyl, aryl, substituted aryl, acyl, (C₁-C₄)alkyl-aryl, (C₁-C₄)alkyl-substituted aryl, heterocycle, substituted heterocycle, (C₁-C₄)alkyl-heterocycle, (C₁-C₄)alkyl-substituted heterocycle, or (C₁-C₄)alkyl-(C₃-C₇)cycloalkyl; or a novel compound of Formula I according to Claim 37, or pharmaceutically acceptable salts thereof,

for the manufacture of a medicamernt for the treatment of diastolic or systolic congestive heart failure or rheumatoid arthritis.